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NON-PROVISIONAL PATENT APPLICATION

METHODS AND APPARATUS FOR ENHANCING DIAGNOSIS OF MYOCARDIAL INFARCTIONS

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METHODS AND APPARATUS FOR ENHANCING DIAGNOSIS OF MYOCARDIAL INFARCTIONS

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This is a regular patent application claiming the benefit under 35 U.S.C. §119(e) from U.S. Provisional Patent Application No. 60/396,681 filed July 17, 2002, the full disclosure of which is incorporated herein by reference.

[0002] Various embodiments of the present invention employ methods, apparatus, and/or systems related to similar methods, apparatus, and/or systems described in PCT Application No. WO 01/67954 A1, filed March 14, 2001, by a common inventor to the present application, the entire contents of which are hereby incorporated by reference. A copy of WO 01/67954 A1 is attached to this application as Appendix A.

BACKGROUND OF THE INVENTION

[0003] The present invention relates generally to diagnosis of myocardial infarctions. More specifically, the invention relates to methods and apparatus for enhancing diagnosis and localization of acute myocardial infarctions using electrocardiogram data.

[0004] Acute myocardial infarction (AMI), commonly known as heart attack, is the single most common cause of death in the US. This disease entity is typically caused by an acute thrombotic event which leads to occlusion of a major coronary artery. When a coronary artery is occluded (i.e., blocked), the portion of the heart tissue which that artery supplies with blood no longer receives sufficient blood to provide oxygen to the tissue. If not quickly treated, this lack of blood supply ("ischemia") results in permanent damage and cell death in the myocardial tissue. Since myocardial damage due to cardiac ischemia becomes irreversible after a certain time, it is imperative that therapy to restore blood flow to the heart be started as quickly as possible. Thus, rapid diagnosis of AMI is also imperative, so that appropriate treatment can be started as quickly as possible.

[0005] Typical therapies for AMI include administering thrombolytic agents intravenously or percutaneous transluminal coronary angioplasty (PTCA) with or without stent placement. In

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either type of therapy, it would be advantageous to have information regarding the location of the AMI on the heart and the identity and/or location of the coronary artery that is blocked. This would allow the medical professional administering the therapy to focus quickly on the affected area for treatment. Information about where on the heart the AMI has occurred and information about the size of the AMI would help a medical professional to determine which artery is occluded and where, along the length of the artery, the occlusion is located.

[0006] The most commonly used, currently available methods and apparatus for diagnosing AMI are the standard 12-lead electrocardiogram (ECG) and biochemical cardiac markers, such as creatine kinase isoenzyme-cardiac muscle sub-unit (CK-MB), tropinin T and I, and myoglobin. Less frequently used diagnostic techniques include computerized 12-lead ECG analysis, nuclear imaging (Technetium-99m-sestamibi), echocardiography, ECG exercise stress testing, continuous 12-lead ECG monitoring, and nonstandard ECG leads (i.e. right precordial chest leads). Despite this large number of option, standard 12-lead ECG and cardiac marker analysis remain the current mainstays of AMI diagnosis in the emergency room, likely due to availability and ease of use.

[0007] The standard 12-lead ECG and cardiac markers each have several shortcomings in their abilities to quickly and accurately diagnose AMI. For example, 12-lead ECG analysis is a relatively fast diagnostic method but generally has low sensitivity and specificity in detecting AMI, particularly in patients with an acute posterior or lateral MI. On the other hand, the most commonly used cardiac markers (i.e. CK-MB and the cardiac troponins) are not released until several hours after the AMI has occurred and, thus, do not provide for rapid diagnosis. Neither the 12-lead ECG nor the cardiac markers typically provide information regarding the location or size of an AMI.

[0008] In an effort to enhance diagnosis of AMI, alternative ECG techniques have been proposed. Some techniques, for example, use greater than the standard number of 12 leads. For example, the PRIME ECG™ device, available from Meridian Medical Technologies, Inc. (Columbia, MD), includes 64 anterior leads and 12 posterior leads disposed in an electrode vest. Such ECG devices cover a larger area on the chest than conventional 12-lead ECGs, which typically improves their ability to accurately detect AMI. As with conventional ECGs, the

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multiple-lead ECGs provide rapid diagnosis, as opposed to the slower diagnostic techniques involving cardiac markers.

[0009] Although multiple-lead ECGs represent an improvement over conventional ECGs, they still have certain drawbacks. Currently available ECG systems, for example, typically detect AMI by comparing the ECG tracings of a patient to a preset baseline tracing. If the patient's tracing differs from the baseline by more than a specified threshold level, then the patient is said to be experiencing an AMI. Unfortunately, this method of diagnosis can at times lack sensitivity, specificity or both. This leads to some patients with AMI being discharged from the hospital without treatment, because their AMIs are not detected, while other patients are treated for AMI, for example with an angioplasty procedure, when they in fact did not have a AMI. Additionally, although multiple-lead ECGs are able to detect AMI accurately in many cases, they do not provide information regarding the location of the AMI on the heart, the size of the AMI, or similar diagnostic information which would help a cardiologist, surgeon or other treating physician to pinpoint and quantify the AMI.

[0010] For the foregoing reasons, it would be advantageous to have methods and apparatus for enhancing diagnosis of AMI. More specifically, it would be advantageous to have improved methods and apparatus for detecting AMI, determining a location of an AMI on a heart, determining the size of an AMI, or any combination thereof.

BRIEF SUMMARY OF THE INVENTION

[0011] The present invention generally uses electrocardiogram data to enhance diagnosis of acute myocardial infarction (AMI). Typically, cardiac data from a patient, acquired from multiple-lead ECG devices (for example, between about 30 and about 130 leads), is compared to stored cardiac data from multiple AMI patients. The stored data also includes information such as presence of an AMI, the location of the AMI on the heart, the size of the AMI, and/or the like. The new patient's ECG can be matched with stored cardiac data that is similar to that of the new patient and, thus, the presence, location, size, and/or the like of the new patient's AMI can be determined.

[0012] Generally, data is acquired from multiple patients, sorted, and stored, so that subsequent patients may be diagnosed based on the stored data. For example, cardiac data for

each patient may include signals from each of multiple ECG leads. The data from the leads are evaluated and reconstructed to create an integral map and a potential map by evaluating a segment, such as the ST segment, of all the signals and plotting them in a grid or similar matrix to create a unique cardiac map for each patient. The data for multiple patients is then sorted, so that patients with similar cardiac data maps are grouped together. The maps are also correlated with locations of ischemia in the patients' hearts, the locations being determined using standard methods such as thallium scans, angiography, and/or other diagnostic tests. When a new patient is evaluated via the multiple-lead ECG, the presence, location and/or size of any AMI in the patient's heart may be diagnosed by comparing the patient's map to the stored data.

[0013]   In one aspect, a method for compiling data to enhance diagnosis of a myocardial infarction includes measuring cardiac data of multiple patients, using a multiple-lead electrocardiogram, sorting the cardiac data into groups, each group comprising cardiac data from one or more patients who experienced ischemia in a similar location on their hearts, and storing the sorted cardiac data. Optionally, the measuring may include acquiring electrocardiogram data from the patients with the multiple-lead electrocardiogram while the patients are suspected to be experiencing ischemia, confirming that the patients experienced ischemia, and identifying at least one location of the ischemia on the heart of each patient. Alternatively, the measuring may include acquiring electrocardiogram data from the patients with the multiple-lead electrocardiogram while the patients are experiencing temporary ischemia during percutaneous transluminal coronary angioplasty, and identifying at least one location of the temporary ischemia on the heart of each patient. In some embodiments, the identified location of ischemia on the ~~hearts~~heart is taken from a group consisting of an anteroseptal location, an inferior location, a posterolateral location.

[0014]   In another aspect, a method for enhancing diagnosis of a myocardial infarction in a patient includes matching cardiac data acquired from the patient with stored cardiac data, wherein the stored cardiac data includes data from multiple ischemia patients sorted into groups of patients based on locations on the ischemia patients' hearts where ischemia occurred, and identifying at least one location of ischemia on the patient's heart, based on the stored cardiac data that matches the acquired cardiac data. In various embodiments, the method may also

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include determining whether a myocardial infarction has occurred in a patient, determining a size of the myocardial infarction, and/or otherwise quantifying the myocardial infarction.

[0015] In yet another aspect, a method for enhancing diagnosis of a myocardial infarction in a heart of a patient includes acquiring cardiac data from the heart using a multiple-lead electrocardiogram device, matching the cardiac data to stored cardiac data for at least one ischemia patient, wherein the location of ischemia on the ischemia patient's heart is known, and displaying information regarding at least one location of ischemia on the patient's heart, based on the matching stored cardiac data for the ischemia patient.

[0016] A system for using stored electrocardiogram data to enhance diagnosis of a myocardial infarction in the heart of a patient may include a data storage module for storing electrocardiogram data of multiple patients, the patients having either experienced a myocardial infarction or temporary cardiac ischemia during percutaneous transluminal coronary angioplasty and the data being sorted according to locations of ischemia on the hearts of the patients, and computer software for enabling comparison of new electrocardiogram data to the stored electrocardiogram data to determine a location of ischemia in the heart of the patient. The system may optionally include a disposable panel including multiple electrocardiogram leads for acquiring cardiac data from a patient. The system may also optionally include a display module for displaying information related to a patient's heart.

[0017] An apparatus for enhancing diagnosis of myocardial infarctions may include a database with stored electrocardiogram data from multiple patients with cardiac ischemia in known locations on the heart, the stored electrocardiogram data being sorted into multiple groups based on the known locations. Alternatively, an apparatus may include a disposable panel or similar device containing multiple electrocardiogram leads for measuring cardiac data in a patient. In other embodiments, an apparatus includes a multiple-lead electrocardiogram panel which may be coupled with a database for diagnosing and localizing ischemia and AMI in a patient.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] Fig. 1A schematically illustrates a sensor system having an array of sensing locations distributed across a patient's torso.

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[0019]   Fig. 1B graphically illustrates the method for calculating an integral value across a selected time portion of a heart signal cycle from a single sensor location.

[0020]   Fig. 1C illustrates a plot of a data matrix generated by mapping the integral values with positions corresponding to the locations of the sensors across the patient's torso.

[0021]   Fig. 2 schematically illustrates a method and computer program for separating a portion of an electrocardiogram signal relevant to a first portion of a heart from signals relevant to alternative portions of the heart.

[0022]   Figs. 3A-D graphically illustrate signal portion separation method steps employed by the program and method of Fig. 2.

[0023]   Fig. 4A graphically illustrates a database of known atrial paced heart cycles as 17 mean P wave integral maps.

[0024]   Fig. 4B and 4C illustrate 17 known right atrial ectopic origins associated with the 17 mean P wave integral maps of Fig. 4A.

[0025]   Figs 5A-C illustrate a database of mean P wave integral maps and associated locations of ectopic origins of the left atrium.

[0026]   Figs. 6A-F illustrate correlations between integral maps of paced heart signal cycles obtained in different patients at a common region in the left atrium.

[0027]   Fig. 7 illustrates a database of QRS integral maps and associated ectopic origins within the right ventricle.

[0028]   Fig. 8 illustrates a database of QRS integral maps and associated ectopic origins within the left ventricle.

[0029]   Fig. 9 illustrates a diagnosis and treatment methodology using an arrhythmia location database and signal separator to help locate and treat the origins of focal AFib and other arrhythmias.

[0030]   Figs. 9A and 9B illustrate arrhythmogenic regions of the left and right ventricles, respectively.

[0031]   Fig. 10 schematically illustrates a system and/or kit for diagnosing and/or treating focal AFib and other arrhythmias, according to the principles of the present invention

[0032]   Figs. 11A-11H illustrate exposed and skin-engaging surfaces of four panels supporting heart cycle sensors in an exemplary sensor array structure.

[0033]   Figs. 12A and 12B are computer screen prints of an AFib localization program showing the localization output.

DETAILED DESCRIPTION OF THE INVENTION

[0018] [0034] The present invention generally provides for enhanced diagnosis of myocardial infarctions, especially acute myocardial infarctions (AMIs). More particularly, the invention provides methods and apparatus for helping medical professionals or other users to detect an AMI, identify a location of the AMI on the heart, and/or determine the size of the AMI. From such determinations, a physician can make a more accurate assessment of which coronary artery is occluded and where treatment should be directed.

[0019] [0035] Most embodiments of the present invention employ multiple-lead electrocardiogram (ECG) devices and/or data from such devices to achieve such enhanced diagnosis. In some embodiments, for example, ECGs with between about 30 and about 130 leads are used to compile a body surface map. One type of ECG device which may be used is described in PCT Application No. WO 01/67954 A1, (hereinafter "'954 application") previously incorporated by reference and attached hereto as Appendix A. Such a device generally includes multiple panels, each panel including multiple ECG leads, which are configured to be placed on, under or around a patient's torso to collect cardiac data. (See, for example, Figs. 11A-11H and accompanying description in '954 application.)

[0036]   The '954 application is directed to techniques for localizing and/or treating atrial fibrillation and other arrhythmias. As explained in the '954 application and illustrated in Fig. 1A, the techniques of the present invention will generally make use of an array 10 of sensors 12 distributed across anterior and posterior skin surfaces of torso T on patient P. Array 10 provides multilead electrocardiogram (ECG) data at a plurality of sensing locations distributed across torso T, typically at over 20 sensing locations, more preferably at over 40 sensing locations, and ideally at 62 or more sensing locations.

[0037] Sensors 12 generally comprise unipolar or bipolar electrodes coupled to the patient's skin, or to an alternative accessible body surface (for example via a transesophageal approach) suitable for measuring electrical body surface potential. Suitable electrode structures may include those described in U.S. Patent Nos. 5,311,873 and 5,634,496, previously incorporated herein by reference. Exemplary arrays for use in locations having large amounts of electromagnetic noise (such as an electrophysiology lab or other location in which electrosurgery or electrical stimulation of tissues for intracardiac pacing is performed) was described by Metting van Rijn, A.C. et al. in IEEE Trans. Biomed. Eng., BME-40:302-308; (1993). Alternative sensor array structures and associated data acquisition and manipulations components were described by SippensGroenewegen, A. et al. in an article entitled, *"Body Surface Mapping During Pacing at Multiple Sites in the Human Atrium: P wave Morphology of Ectopic Right Atrial Activation"*, Circulation, 97:369-380 (1998); and by Linnenbank, A.C. in a 1996 thesis for the University of Amsterdam entitled, *"On-Site Recording, Analysis, and Presentation of Multi-channel ECG Data"*.

[0038] Referring now to Fig. 1B, ECG data is preferably acquired simultaneously from each sensor 12 of array 10 at a sampling rate of over about 500 Hz, ideally at a sampling rate of about 1,000 Hz or more. In some embodiments, sequential sampling of sensor 12 from array 10 may alternatively be used, and higher or lower sampling rates are also feasible. When a lower sampling rate is used, the data may be upsampled using multi-rate filter banks.

[0039] Preferably, signals which are absent, for example, due to electrode obscurement by defibrillator patches or lead dislodgment, may be deleted. Poor quality signals may also be visually and/or automatically identified and rejected. Such rejected signals may be replaced using interpolation of adjacent lead recording data. Interpolation techniques may also be utilized to correct for offset variation among electrodes, and for linear baseline drifting.

[0040] Graph 14 includes an ECG signal tracing 16 representing the variation in voltage over time, as sensed by sensors 12, optionally at about 1 to 2 ms intervals. Signal tracing 16 may be used to evaluate heart cycle signals from the heart of patient P. In general, one or more reference heart cycles will be selected for manipulation and comparison. The reference heart cycle will typically be the heart cycle coinciding with initiation of the arrhythmia for localizing focal AFib, or a premature heart cycle that has the same morphology as the cycle that led to initiation of

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focal AFib. ECG Tracing 16 can be used to determine a beginning 18 and end 20 of a time portion 22 of the reference heart signal cycle which is of particular interest for evaluating one or more regions of the heart. In the example illustrated in Fig. 1B, a P wave onset may be determined by the time at which the voltage progresses beyond 30 µV while termination of the P wave may be defined at the atrial J-point, as is generally understood in the field of electrocardiography. Alternative criteria for P wave onset and offset might also be utilized, and automated detection of time portion 22 is also feasible. Alternative time portions may also be selected.

[0041] Referring to Figs. 1B and 1C, measurements made at each sensor 12 are preferably mapped onto a data matrix 24 according to the locations of the associated sensor. In the exemplary embodiment, a P wave integral numerical value 24 may be calculated based on heart cycle signals 16 within selected time portion 22 for a particular sensor location N10. This calculated P wave integral value reflects the time/amplitude area of ECG signal at that sensor location within the selected time portion. Similar integral values are calculated for each sensor location, and the sensor values are mapped within data matrix 24 continuously from a portion of the data matrix associated with a front F of torso T, across a side of the patient P, and to a back B portion of torso T. As shown in Figure 1C, the data matrix will often be presented graphically by calculating lines of constant integral values 28 based on the individual discrete integral values and their associated positions within the data matrix. In some embodiments, this information can be summarized by presenting a single line 30 of zero integral value between a region of positive integral values 32 and a region of negative integral values 34. In much of the description which follows, the region of positive integral values 32 is presented as a shaded region within a graphically depiction of data matrix 24. Exemplary alternative data matrices may be presented with shades of a first color (red, for example) for positive values, a second color (blue, for example) for negative values, and optionally a third color (such as green) for zero.

[0042] For localizing of certain arrhythmias, possibly including certain ventricular tachycardias and some types of atrial tachycardia, directly using measurements from sensors 12 to calculate integral values 26 for the selected time portion 22 maybe sufficient to identify an arrhythmogenic region (which may be relatively large) of a particular ventricle, and in some cases, a particular atrium. Localizing directly from the sensed heart cycle signals is significantly

facilitated when the signals within the time portion of interest are predominantly indicative of activity within a candidate ectopic region of the heart. For example, when localizing ventricular tachycardia (VT), selecting a time portion dominated by the QRS complex in the signal can effectively localize arrhythmogenic foci or exit site, as more fully described in the J. Am. Coll. Cardiol., 24:1708-1724 (1994), the full disclosure of which is incorporated herein by reference. This localizing of tachycardia foci within the ventricle may be facilitated by the domination of the QRS complex in the signal of the overall body surface potential.

[0043] Unfortunately, when localizing fibrillation foci within an atrium, the P wave (which can be indicative of activity within the atrium) will often be superimposed, either partially or completely, by the T-U wave. Physiologically speaking, the atrial activity of interest may coincide with ventricular recovery of the preceding cardiac cycle.

[0044] To accurately localize focal triggers during the initiation of paroxysmal or persistent AFib, the present invention makes use of systems and methods for effectively separating a signal portion of interest from a superimposed signal portion, with the two signal portions often being separated from a single signal sensed from at least one single sensor location. These signal separation techniques are particularly advantageous when used to isolate the P wave from a simultaneously occurring T-U wave. It may be possible in some circumstances to artificially separate these waves by active overdrive pacing using an intracardiac catheter with a pacing period selected to avoid superimposition of these two signal portions during artificially initiated arrhythmia. For the reason described above, non-invasive electrocardiographic localization of atrial arrhythmias, particularly atrial premature beats before or during invasive mapping procedures is highly advantageous. As will be understood with reference to Figs. 2 – 3D, a QRST subtraction program helps to isolate and preserve the P wave morphology so as to enable trigger localization of focal AFib and other arrhythmias. The application of similar subtraction methodologies may also enhance the ability of body surface mapping systems to localize triggers, exit sites, pathway insertion points, flutter waves, and/or fibrillation waves of other atrial arrhythmias such as atrial flutter, chronic AFib, and the like. QRST subtraction program 40 may also enable application of inverse problem techniques to analysis of atrial arrhythmias, for example, when atrial depolarization is obscured by the preceding ventricular repolarization. It should be understood that alternative signal separation methods and systems might also be

used, including those described in the following references, which are incorporated herein by reference: Slocum, J. et al., *"Computer Detection of Atrioventricular Dissociation from Surface Electrocardiograms During Wide QRS Complex Tachycardias,"* Circulation, 72:1028-1036 (1985); Slocum, J. et al., *"Diagnosis of Atrial Fibrillation from Surface Electrocardiograms Based on Computer-Detected Atrial Activity,"* J. Electrocardial., 25:1-8 (1992); Holm, M. et al., *"Non-Invasive Assessment of the Atrial Cycle Length During Atrial Fibrillation in Man: Introducing, Validating and Illustrating a New ECG Method,"* Cardiovasc. Res., 38:69-81 (1998); Bollman, A. et al., *"Frequency Analysis of Human Atrial Fibrillation Using the Surface Electrocardiogram and its Response to Ibutilide,"* Am. J. Cardiol., 81:1439-1445 (1998); and Ingemansson, M.P. et al., *"Autonomic Modulation of the Atrial Cycle Length by the Head Up Tilt Test: Non-Invasive Evaluation in Patients with Chronic Atrial Fibrillation,"* Heart, 80:71-76 (1998).

[0045] Referring now to Fig. 2, automated QRST subtraction program 40 uses an adaptive QRST template constructed from averaged QRST complexes combined with ECG body surface measurements to enable isolation of the otherwise obscured ectopic atrial activity. Generally, this approach allows the surface ECG measurements to retain their intricate spatial and temporal detail within the P wave morphology. Subtraction program 40 is capable of unmasking and preserving subtle heart signal details of relatively low voltage P wave signal portions despite the obscuring superimposed relatively high voltage QRST complex. The QRST subtraction method of Fig. 2 is described in more detail in U.S. Patent Application No. 60/189,513 filed March 15, 2000, previously incorporated herein by reference.

[0046] As described above, the method of program 40 generally includes recording of unipolar ECG data from the array of torso sites in step 42. The measured signal will include both the P wave (which is of interest for AFib) and a superimposed QRST signal portion 44.

[0047] In the exemplary embodiment, about 100 cardiac cycles of 62-channel ECG data are measured during sinus rhythm or atrial overdrive pacing. Optionally, ECG signals can be acquired during both sinus rhythm and atrial pacing. Fewer cycles may be used if the spatial and temporal variations of the QRST complex are relatively low. Typically, more than ten (10) cycles will be used, often more than 50 cycles for construction of the QRST template. As illustrated in Fig. 3A, off-line digital filtering of the data designated for template construction

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may be performed using a 0.5 Hz high-pass filter, such as an IIR Chebychev Type-1 filter. This can help to correct for respiration-related baseline drifting. Additionally, a 100 Hz low-pass filter, such as a IIR Chebychev Type-1 filter, may be used to remove high-frequency signal artifacts. Additionally, a 50-60 Hz notch filter may be used to remove line-frequency interference. Similar filtering may be employed on the superimposed signals to be separated.

[0048]　Each filtered QRS complex 48 may be identified using a complex-resonator/comb filter, together with a dual-edge threshold detection technique similar to that described by Ruha, A. et al., in an article entitled *"A Real-Time Microprocessor QRS Detector System with a 1-ms Timing Accuracy for the Measurement of Ambulatory HRV"*, IEEE Trans. Biomed. Eng., 44:159-167 (1997), the disclosure of which is incorporated herein by reference. Alternative QRS detection methods might also be used.

[0049]　R wave fiducial points are marked and the average R-R interval is computed. The dominant QRS morphology is identified, optionally using visual identification from pooled data, automated statistical methods, or the like. This dominant QRS morphology is used to select complexes for template creation.

[0050]　QRST template construction 50 may be understood with reference to Fig. 3B. The selection of complexes for template creation may be based on two criteria: QRS pattern, and R-R interval length.

[0051]　Regarding QRS pattern criteria, complexes of each cycle are compared with the template using parametric cross-correlations. In the exemplary embodiment, Pearson's coefficients are computed for a fixed time window sliding over a 20 ms time period. Once again, a variety of alternative cross-correlations may be used. Each newly selected complex (for example, those having $r \geq 0.98$) is aligned and averaged with previously selected cycles, and the QRS template is updated. Each complex which does not have adequate correlation with the template is excluded, with these complexes often being ectopic or aberrantly conducted ventricular beats.

[0052]　Minimum R-R duration threshold is computed and only complexes having an R-R duration above the computed threshold are used to create the QRST template. For each complex, the Q wave fiducial point is identified and the average Q-R interval is computed. The average

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Q-T interval (the length of the QRST complex) is computed, optionally using a modified Bazett's formula. Additional correction for baseline drifting may be performed using linear interpolation after averaging a window prior to the Q wave. An adaptive template may be constructed from the selected complexes by averaging their QRST intervals, optionally with the complexes aligned by a window surrounding the R wave fiducial point.

[0053] In step 52, the above-described fiducial window in the QRS complexes, together with an additional fiducial time window around the peak of the T wave, are marked automatically. These fiducial windows are marked in both the QRST template, and in the superimposed signal 48 containing a QRST complex together with a superimposed P wave.

[0054] In step 54, the template 56 and the superimposed signals are aligned. Typically, T wave window onset for the template is estimated as 0.64*QT. The T wave window is adjusted for each complex based on the QT interval length. Optionally, the operator can manually adjust any fiducial marker, such as by manipulating a mouse, joystick, by putting a numerical value, or the like, the template's QRS fiducial points and T wave windows are aligned with the respective windows of the superimposed QRST complex. Alignment of superimposed signal 48 and template 56 may be performed manually, or automatically by sliding windows over each other in 10-ms increments and calculating cross-correlation coefficients.

[0055] After alignment of the fiducial windows, the template is resampled as well as amplitude modulated 58, and then QRST subtraction is carried out as can be understood with reference to Fig. 3D and step 60. Template resampling and modulation are performed to compensate for discrepancies in duration (as a result of rate-related differences in the QRST interval) and amplitude (as a consequence of variations in peak R-T wave voltage, which may be predominantly caused by respiratory variation). This process is particularly geared toward obtaining optimal subtraction performance of the T-U wave complex. Optionally, cubic spline interpolation methods may be used for template resampling, although other multi-rate processing methods can also be used.

[0056] The subtraction procedure from channel-to-channel may be performed according to electrode position. This facilitates maintaining sliding intervals as small as 10 ms while having the Q-T interval dispersion accessed in multiple leads. Additional low-pass filtering can be carried out to smooth possible QRS leakage after QRST subtraction. The remaining ECG signal

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after QRST subtraction features a P wave which is effectively isolated from the previously superimposed T-U wave.

[0057]   After the QRST segment is effectively subtracted from each measured signal containing a P wave of interest, the morphology of the isolated P wave can be analyzed as described above. Specifically, an integral map may be computed of the separated, previously superimposed P wave. This integral map can be compared with a database of P wave maps created by pacing, so that atrial tachycardia, atrial accessory pathway insertion sites, and focal triggers of paroxysmal or persistent AFib may be localized using data from the surface ECG array 10, as shown in Fig. 1A. Advantageously, the method described herein above may obtain high performance in the T-U wave range by correcting specifically for differences in both the QRST duration, and in the voltage of the T wave. Additionally, the above-described QRST subtraction methodology makes use of a separate data set than the superimposed wave to be separated, with the separate data set optionally being obtained during sinus rhythm or atrial overdrive pacing to help insure that atrial and ventricular activity are clearly separated. As was also mentioned above, the superimposed wave or reference cycle of interest will often comprise a single ectopic atrial heartbeat which can be readily separated using the above-described method.

[0058]   Once the signal separation has been successfully completed for the reference heartbeat at each sensor location 12 of array 10, a P wave integral map may be plotted from the data matrix 26 as described above with reference to Figs. 1A-C. Similar QRS integral data matrices and plots may be generated for localizing ventricular arrhythmias.

[0059] In many embodiments, data from such multiple-lead ECGs are used to create body surface maps, which are compared with stored body surface maps of multiple AMI patients. Again, for descriptions of similar body surface mapping methods and apparatus, in the context of cardiac arrhythmias, see the '954 application. In other embodiments, similar cardiac data is used, but the stored body surface maps are taken from patients who ~~experiences~~experience temporary cardiac ischemia while undergoing angioplasty procedures.

~~[0020]~~[0060] Various embodiments of a method for enhancing diagnosis of AMI suitably include first collecting cardiac data. For example, in some embodiments, cardiac data may be acquired from patients undergoing percutaneous transluminal coronary angioplasty (PTCA). Cardiac data may be acquired using any suitable multiple-lead ECG device, but as discussed

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briefly above, various embodiments employ one or more disposable panels, each of which contains multiple ECG leads. Disposable panels will generally be configured to be placed on, under or around a patient to measure ECG signals with the leads. When a PTCA patient is being treated, he or she will undergo a temporary cardiac ischemia when the angioplasty balloon or similar device is inflated. Cardiac data may be measured during that time, and a map made of that cardiac data may be correlated with the known area of ischemia. The area of ischemia is known, of course, because the surgeon or other physician conducting the PTCA procedure knows where the angioplasty balloon is located when it was inflated.

[0021] [0061] In other embodiments, patients suspected of having an AMI could be assessed with an ECG device, such as the panels just described. The presence, location and/or size of the AMI could then later be confirmed by cardiac marker analysis, thallium scan, cardiac angiography, and/or other diagnostic methods. Angiography, echocardiography, and/or any other suitable studies may be used to provide further information about the AMI in each patient's heart. For example, the exact location of the AMI on the heart, the occluded coronary artery, the quantity of heart tissue affected by the AMI, and/or the like could be determined. This information could then be stored, along with ECG data, for each patient. In some embodiments, the information regarding the AMI and the ECG data will be processed to determine ECG characteristics that relate to AMI characteristics. For example, a particular ST elevation on an ECG may correspond to a particular location for an AMI in multiple patients. Such correlated information and data may then be used by medical professionals to more specifically diagnose AMI.

[0022] [0062] In various embodiments, then the multilead ECG data will be used to create surface mapping of hearts for use in AMI diagnosis. Typically, such maps will be based on the following three sets of data or characteristics, though some embodiments may include less than all three: (1) infarct detection (rule in/rule out MI); (2) infarct localization (risk assessment to determine nature of acute treatment); and (3) infarct quantification (risk assessment to determine nature of acute treatment). Techniques for mapping are discussed in more detail in the '954 application previously incorporated by reference.

[0063] The '954 application is directed to techniques for localizing and/or treating atrial fibrillation and other arrhythmias. As explained in the '954 application and illustrated in Figs.

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4A-C, a graphical plot of a particular patient's P wave integral may be used to localize an arrhythmogenic region in an atrium by comparing the P wave integral plot for the patient to a database of P wave integral plots having associated known ectopic foci within the right atrium. Each of the 17 plots of database 70 has an associated ectopic region (identified by the encircled numbers illustrated in Figs. 4B and 4C), the database having been gathered using pacing.

[0064]   The anterior-posterior view AP shown in Fig. 4B and the posterior-anterior PA view of Fig. 4C illustrate the right atrial cavity. Anatomical landmarks included in these diagrams include the superior vena cava SVC, and inferior vena cava IVC; the right atrial appendage RAA; the smooth right atrium SRA; the trabeculated right atrium TRA; the crista terminalis CT; the fossa ovalis FO; the left atrium LA; the Eustachian valve EV; the coronary sinus os CSO; the tricuspid valve TV; the right pulmonary artery RPA; and the left pulmonary artery LPA. Methods for assembling a right atrial database are described in detail in the J. Electrocardiol., 31 (Supp.):85-91 (1998), previously incorporated herein by reference. A similar left atrial database 80a, b, and c (generally referred to as left atrial database 80) is illustrated in Figs. 5A-C. Once again, the encircled numbers relate mean P wave integral plots to specific endocardial regions of pacing shown in the anatomical diagrams.

[0065]   The mean P wave integral maps of left and right atrial databases 70, 80 feature extreme positions and zero line contours without positive and negative integral contour lines. Alternative plot formats, such as three-dimensional or chest anatomy-based formats, map displays using various color schemes, and the like, may also be used.

[0066]   The anatomical diagrams illustrated in Figs. 5A-C present a posterior-anterior PA view and anterior-posterior AP view, and a left posterior-oblique LPO view of the left atrium LA. Once again, major anatomical landmarks are highlighted including the left and right pulmonary arteries LPA, RPA; the superior and inferior vena cava SVC, IVC; the left atrial appendage LAA; the right atrium RA; the coronary sinus CS; the left ventricle LV; the left upper pulmonary vein LUPV; the left lower pulmonary vein LLPV; the right upper pulmonary vein RUPV; the right lower pulmonary vein RLPV; Bachmann's bundle BB; the mitral annulus MA; the anterior mitral valve leaflet AMVL; and the fossa ovalis FO.

[0067]   Referring now to Figs. 6A-F, six individual P wave integral maps included within group 6 were each obtained during pacing at the left upper and left lower pulmonary veins.

These six similarly located pacing sites were grouped together within group 6 of left atrial database 80, and these plots were averaged to produce the sixth numbered mean plot of the left atrial database. The spatial compatibility of these patterns can be clearly seen, particularly with reference to the location and orientations of both the highest positive and negative integral values, as well as with reference to the zero line contour separating the shaded from unshaded regions. While each of these six patient-specific maps were generated using intracardiac pacing, naturally occurring ectopic origins may be identified by comparing reference heart cycle signals measured during premature atrial beats, the onset of AFib, and/or atrial tachycardia (and optionally separated from superimposed signals described above) to these mean paced plots.

[0068] Referring now to Figs. 7 and 8, a right ventricular database 82 and a left ventricular database 84 each include mean QRS integral maps for paced ectopic origins in the right and left ventricles, respectively. These ventricular databases are more fully described in an article by *Peeters, H.A.P. et al.* entitled *"Clinical Application of an Integrated 3-Phase Mapping Technique for Localization of the Site of Origin of Idiopathic Ventricular Tachycardia"*, Circulation 99:1300-1311 (1999) the disclosure of which is incorporated herein by reference.

[0069] Referring now to Fig. 9, a localization/treatment method 100 may be performed by first establishing a database of arrhythmogenic regions and associated heart cycle signal characteristics, as described with reference to Figs. 4A-8 above. Body surface measurements are taken in step 102, typically using sensor array 10 described with reference to Fig. 1A. As the P wave will often overlap other heart signal portions, localization of AFib and other arrhythmias will benefit from a signal separation program as described above regarding Figs. 2-3D.

[0070] Once signal separation has been effected, P wave integrals (or other selected indicia) are determined for each sensor 12, and data matrices assembled as described with reference to Figs. 1B and 1C. Once again, it should be understood that these P wave integrals are calculated for a reference heart cycle signal of interest, usually for a premature atrial beat or for the heart cycle signal at the onset of an arrhythmia, for focal arrhythmias. Optionally, the data matrix may be compared with the plots of the established database in step 104. This database comparison method may simply involve visually selecting the mean-paced integral map which appears most similar to the plot for a specific patient. Alternatively, statistical correlation coefficients may be generated between the data matrix for the patient and each of the mean-paced groups of the

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database. In some embodiments, different patient plots may be prepared for comparison with different databases, for example, a P wave integral may be calculated for comparison with atrial database groups, while a QRS integral plot may be prepared for comparison with ventricular database groups.

[0071] Once a mean-paced integral plot from the database has been selected as the closest correlation to the reference cycled plot for a particular patient, an arrhythmogenic region 106 associated with the corresponding mean-paced plot has effectively been identified. Arrhythmogenic regions 106 associated with mean-paced plots 1-25 of left ventricular database 84 and plots 1-13 of right ventricular database 82 are illustrated in Figs. 9A and 9B, respectively. In many embodiments, these arrhythmogenic regions will be discrete locations based on the information within the associated database. Preferably, arrhythmogenic regions 106 will have surface areas of less than about 5 cm^2. Optionally, the arrhythmogenic regions may have an outer radius which is less than about 2.5 cm, ideally about 1.0 cm or less. In some embodiments, the arrhythmogenic regions identified by sensor array 10 on the patient's torso may be small enough that no further localization is needed, and ablation of the ectopic site or exit site within the arrhythmogenic region may proceed without excessive collateral damage.

[0072] Referring now to Figs. 9 and 10, once an arrhythmogenic region 106 has been identified, it will often be advantageous to further localize an ectopic origin or exit site 108 within arrhythmogenic region 106 using a pace mapping catheter 110. Advantageously, this mapping of ectopic origin or exit site 108 may proceed rapidly within the limited confines of the arrhythmogenic region 106, thereby reducing fluoroscopy time and radiation exposure to patient and attending personnel, decreasing the trauma associated with accessing alternative portions of heart H, and the like. In general, pace mapping is effected by electrical stimulation of candidate ectopic origins within arrhythmogenic region 106 using a distal electrode pair of catheter 110. This can induce ectopic heart beats which can also be measured by array 10 (or a similar array adapted for use in a high electromagnetic noise environment). Positioning of the catheter tip may be monitored using biplane x-ray imaging.

[0073] The surface ECG corresponding to the paced beats is recorded, and the desired integrals and associated data matrix is generated, as described above. By comparing the data matrix plot of the induced arrhythmia to the database and/or original arrhythmia recordings, the focal origin

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or exit site of the arrhythmia relative to the catheter position can be estimated, optionally using the method described in U.S. Patent No. 5,311,873, previously incorporated herein by reference. The catheter may be moved to the indicated alternative site, and the pacing and measurement steps repeated iteratively until the ectopic site is found where the paced data matrix plot best correlates with the data matrix plot of the arrhythmia. Once again, this iterative process is greatly expedited by concentrating the ectopic origin or exit site search within arrhythmogenic region 106 identified using sensor array 10.

[0023] [0074] Once maps are made for multiple patients, the maps may be sorted and stored. In many embodiments, for example, maps are generally stored according to the location, on each patient's heart, where ischemia occurred. In very general terms, when a new patient is then diagnosed using a multiple-lead ECG device, data from the new patient can be compared with data from previous patients to determine where the new patient's ischemia is located, whether the patient is actually suffering an AMI, the size of the AMI and/or the like.

[0024] [0075] For example, in some embodiments criteria for AMI detection will be developed based on the analysis of 62-lead ST integral or potential maps. Such ST maps will typically be developed using the presence of a specific amount of ST elevation (for example > 0.1 mV ST elevation) in a required minimum number of chest leads (for example at least 2 leads in the complete array). These data can be obtained by acquiring prospective surface ECG mapping data in a number of patients with AMI documented by cardiac marker analysis and/or coronary angiography. This will enable an assessment of the specific level of ST elevation and the precise minimum number of chest leads required to ensure the highest sensitivity and specificity for AMI detection. In addition, the information provided by the number of leads showing reciprocal ST depression during acute ischemia may also be utilized. As an alternative to the use of ST integral or potential maps, information provided in other segments of the ECG (i.e. QRS complex or QRST segment) may also be used.

[0025] [0076] In many embodiments, a set of stored data such as database of 62-lead ST integral or potential maps will be developed based on a differentiation of the three major infarct regions/locations of the left ventricle which each relate to the major coronary arteries. These regions are: (1) anteroseptal MI (ASMI) due to an occlusion in the left anterior descending (LAD) coronary artery; (2) inferior MI (IMI) due to an occlusion in the right coronary artery

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(RCA); and (3) posterior or lateral MI (PMI or LMI) due to an occlusion in the left circumflex coronary artery (LCx). The locations of these infarct regions can be verified using coronary angiography, for example. The classification in IMI may also include the presence or absence of right ventricular infarction (high-risk versus low-risk patient), which again may assessed using coronary angiography. Using methods of various embodiments of the present invention, infarct regions/locations will be specifically related to an area on the chest where a particular ECG change is measured. In some embodiments, for example, the infarct regions will be related to areas on a chest where ST elevation and/or reciprocal ST depression occurs during a specific time instant in a potential map or during a given time interval in an integral map.

[0026] [0077] As described briefly above, in alternative embodiments, other methods are used to develop the above-described relationships between infarct regions and areas on the chest of ECG change. In some embodiments, for example, 62-lead ECG map patterns may be obtained during percutaneous transluminal coronary angioplasty (PTCA) performed in patients with coronary artery stenosis. In this approach, PTCA is be used as a surrogate model of AMI. At the time when a coronary stenosis is dilated during a PTCA, the vessel occlusion caused by balloon inflation results in temporary transmural ischemia which will generate an ECG pattern similar to the pattern obtained during ischemia caused by AMI. Acquisition of the ECG data during PTCA enables direct correlation of the map patterns with the angiographically validated balloon occlusion site. As an alternative to the use of ST integral or potential maps, information provided in other segments of the ECG (i.e. QRS complex or QRST segment) may also be used.

[0027] [0078] In some embodiments of the invention, information on the size of myocardial infarcts at each of the three major infarct locations (i.e. LAD, RCA, and LCx) will be obtained by developing criteria for analysis of 62-lead ST integral or potential maps that enable differentiation between patients with a proximal occlusion versus a distal occlusion of the infarct-related artery. In some embodiments, further differentiation may be made, for example by differentiating between proximal, middle, and distal occlusions. The location of a proximal versus a distal occlusion of the infarct-related artery may be verified using coronary angiography. As an alternative, PTCA may again be used as a surrogate model of AMI. Acquisition of the ECG data during PTCA would enable direct correlation of the map patterns with the angiographically validated proximal or distal balloon occlusion site.

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[0028]-[0079] In various other embodiments, criteria may be developed for patients with non-ST elevation MI, patients with left (LBBB) or right (RBBB) bundle branch block, left ventricular hypertrophy (LVH), previous (i.e. old) myocardial infarction and/or the like. As with the criteria already discussed, these additional criteria may be determined by examining AMI patients via coronary angiography or by examining PTCA patients. Data from such examinations may then be used to derive criteria related to ECG data.

[0029]-[0080] Once data are collected and one or more sets of criteria for multiple-lead ECG diagnosis of AMI are developed, the data and criteria may be provided to medical professionals in any of a number of suitable forms, to enhance the diagnosis of AMI. In some embodiments, for example, a 62-lead ECG or other ECG device may be coupled with a database such that ECG data collected for a given patient may be quickly compared with data and/or criteria stored in the database. Such comparisons may enable the 62-lead ECG to detect an AMI, determine a location of an AMI, determine a size of an AMI and/or the like.

[0081] Figs. 11A-H illustrate skin-engaging and outer surfaces of four flexible sensor panels. These panel structures and the use of their array or sensors are more fully described in U.S. Patent Application No. 09/611,179, filed on July 6, 2000, (now U.S. Patent No. 6,584,343) the disclosure of which is incorporated by reference in the '954 application, previously incorporated by reference.

[0030]-[0082] Typically, methods and apparatus of the present invention will provide for display of at least one diagnostic characteristic. For example, in many embodiments the detection of an AMI will be displayed, a location of the AMI will be displayed, and a size of the AMI will be displayed. In other embodiments, an occluded vessel may be listed or displayed and/or a section of the vessel which is occluded may be displayed. Display may be accomplished by any suitable means, such as an LCD screen, a computer screen, and the like. For example, display techniques such as those described in the '954 application may be used. (See,see for example, Figs. 12 A-B.).

[0083] The '954 application is directed to techniques for localizing and/or treating atrial fibrillation and other arrhythmias. As explained in the '954 application and illustrated in Figs. 12A and 12B, screen prints 150a, 150b are at least a portion of the output of a localization computer program as described herein. Integral maps 152 are multi-color graphical

representations of the morphology derived from body surface potential maps 154 (also displayed in a multi-color format). Time portion 156 of reference cycle 158 is shown graphically, and may be separated from a superimposed signal by inputting a "subtract" command 160, ideally using a graphical user interface. Identified arrhythmogenic sites 12 are output with their associated probabilities, and are graphically illustrated 164 relative to the adjacent anatomy. In the exemplary output, candidate sites of a selected database are also shown, with one or more of the identified sites being highlighted using color, blinking, an enhanced font or icon, or the like. Optionally, cycle signals from different recorded segments 166 may be selected, and the cycles of interest may be time scaled or zoomed 168 to show the desired cycle intervals. Signals from selected leaps or sensor panels may be displayed, and a variety of additional outputs may be provided. In the output illustrated in screen prints 150a, 150b, two different reference cycles from different arrhythmia events result in similar identified arrhythmogenic sites. Hence, the present invention can also provide confirmation of an arrhythmogenic site identification from one or more confirmation reference cycle.

[0084] In some embodiments, ECG readings of a patient include intuitive display formats in anatomical models of the heart. Existing imaging techniques may be used to verify the infarct location or infarct-related artery. Such techniques include, but are not limited to, coronary angiography (coronary artery anatomy assessment), nuclear imaging (regional perfusion assessment), and echocardiography (wall motion assessment).

[0031] [0085] Although the above is a complete description of a number of exemplary embodiments of the invention, other embodiments, as well as variations of the described embodiments, are also contemplated within the scope of the present invention. Therefore, the foregoing description is intended for exemplary purposed only and should not be interpreted to limit the scope of the invention as it is described in the appended claims.

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